REMARKS

I. STATUS OF THE CLAIMS

Claims 88-89, 92, 94-99, and 109-117 are presently pending with entry of this Amendment. Claims 100-108 were previously withdrawn. Claims 90, 91, and 93 have been canceled herein without prejudice to subsequent renewal or filing in a continuation or divisional application. Applicants reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications, and that claim amendments or cancellations should not to be construed as abandonment of any previously claimed subject matter. Claims 88-89 and 92 have been amended, and new claims 109-117 have been added. The amendments to the claims and the new claims are fully supported by the specification as filed and no new matter has been added. Support for the amendment to claim 88 is provided throughout the specification, including at, *e.g.*, but not limited to, page 20, line 14 to page 22, line 12; page 101, line 1 to page 104, line 9 (*e.g.*, Examples 5-8); and page 108, line 4 to page 120, line 4 (*e.g.*, Examples 14-23). Claim 89 has been amended for consistency with amended claim 88. Claim 92 has been amended to depend from claim 88, as claim 90 has been canceled. Support for the new claims 109-115 is provided throughout the specification, including at, but not limited to, *e.g.*, page 22, line 7 to page 23, line 18. Support for new claims 116-117 is provided throughout the specification, including at, but not limited to, *e.g.*, page 22, lines 17-22 and page 23, lines 4-18.

II. NEW TITLE

Applicants have amended the title herein to one which is clearly more indicative of the invention to which the claims are directed, as suggested by the Examiner.

III. REJECTIONS UNDER 35 USC § 112, SECOND PARAGRAPH

Claims 88-99 were rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention. Office Action, page 3. Specifically, the Examiner finds that independent claim 88 is vague and indefinite because the term "interferon β activity" is not defined in the specification and thus the metes and bounds of claim 88 and claims dependent

thereon are unclear. *Id.* The Examiner states that interferon β is known to have diverse activities such as antiviral, antiproliferative, and immunomodulatory activities, and it is unclear what activity is being contemplated in claim 88. *Id.* at pages 2-3. Claims 89-99 were rejected insofar as they are dependent on rejected claim 88.

The rejection of claims 90-91 and 93 has been mooted by cancellation of those claims without prejudice. The rejection of claims 89, 92, and 94-99 is respectfully traversed. The term "exhibiting interferon β activity" in claim 88 is expressly defined in the specification, *e.g.*, at page 16, line 20 to page 17, line 8. As noted therein, the term is intended to indicate that the polypeptide has one or more of the functions of human wild-type interferon-β (IFN-β) (SEQ ID NO:2), such as the ability to bind to an interferon receptor that is capable of binding IFN-β and initiating intracellular signaling from the receptor (*e.g.*, a type I interferon receptor constituted by the subunits IFNAR-2 and IFNAR-1), antiviral, antiproliferative or immunomodulatory activity. The specification explains that IFN-β activity may be assayed the methods exemplified in the materials and methods section, which is presented in the Examples section (pages 83-120). The specification further explains that a polypeptide exhibiting or having IFN-β activity is considered to have such activity when it displays a measurable function, such as, *e.g.*, a measurable receptor binding and stimulating activity as determined, *e.g.*, by the primary or secondary assay in the materials and method section (see page 84, lines 1-30). Numerous Examples present exemplary IFN-β polypeptide variants that exhibit IFN-β activity as determined by such assays (*see, e.g.*, Examples 5-9, 13-15, *etc.*). Based upon the explicit specification's teachings, one of ordinary skill in the pertinent art would have plainly understood the term "exhibiting interferon β activity." Withdrawal of the rejection is respectfully requested.

IV. REJECTIONS UNDER 35 USC § 112, FIRST PARAGRAPH

A. The Claims Meet the Written Description Requirement

Claims 88-99 were rejected under 35 USC § 112, first paragraph, as allegedly containing subject matter that was not clearly described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed,

had possession of the claimed invention. The Examiner notes this is a written description rejection. Office Action, page 3. Specifically, the Examiner takes the position that:

> The specification discloses several potential interferon-β substitutions at wild-type positions including S2N+N4T+C17S+K19R+K33R+K45R+Q51N+ E53T+F111N+R113T+K123R. This meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose all possible variants (with up to 15 amino acid residue changes) of interferon-β. Applicants have claimed a genus of polypeptides that have no common function (interferon-β has antiviral effects anti proliferative effects *etc.*). It is not clear what substitutions will retain common functions. It is also not clear how the changes to the polypeptide would affect the glycosylation. Furthermore, the specification fails to disclose if there are multiple glycosylation sites and how amino acid substitution next one site [sic] will affect the other *etc.* It is also not how [sic] and what functions will be affected by the glycosylation. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of SEQ ID number and some possible amino acid changes (amino acid changes at up to 15 positions). There is not even identification of any particular portion of the structure that must be conserved. The claims as written, however, encompass interferon-β variant sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 88-99. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Id. at pages 3-4.

The Examiner finds that only the interferon-β polypeptide variant "with substitutions at wild-type positions S2N+N4T+C17S+K19R+K33R+K45R+Q51N+E53T+F111N+ R113T+K123R but not the full breadth of the claims (with all possible amino acids changed) meets the written description provision of 35 USC 112, first paragraph." *Id.* at page 5. The

Examiner contends that the "species specifically disclosed are not representative of the genus because the genus is highly variant" and "[a]s a result, it does not appear that the inventors were in possession of various polypeptide sequences set forth in claims [sic] 88." *Id.* Claims 89-99 were rejected because they depend from claim 88. The rejection of claims 90-91 and 93 has been mooted by cancellation of those claims without prejudice. The rejection of claims 89, 92, and 94-99 is respectfully traversed in part and overcome in part as follows.

The Federal Circuit has discussed the written description requirement in reference to inventions involving a chemical genus. *See Univ. of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Lilly*, the Court explained:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus . . . However, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. *It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.*

Id.

The *Lilly* Court further explained that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Id.* at 1567, 43 USPQ2d at 1405. The Court noted that ***"[a] description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."*** *Id.* at 1568, 43 USPQ2d at 1406.

The Federal Circuit further clarified the written description requirement in the context of DNA-related inventions in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). In *Enzo*, the Court explained that "the written description requirement can be met by 'showing that an invention is complete by disclosure of ***sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'***" *Id.* at 1324, 63 USPQ2d at 1613 (citing the USPTO's Written Description Guidelines, 66 Fed. Reg. 1099 *et seq.*, 1106 (Jan. 5, 2001)) (emphasis added). Notably, the *Enzo* Court adopted the standard for determining compliance with written description set forth in the USPTO's Written Description Examination Guidelines, which apply to protein sequences and DNA sequences.

Recently, the Federal Circuit reiterated the standard articulated in *Enzo*, stating that the written description requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular structure. *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1320, 66 USPQ2d 1429, 1438-39 (Fed. Cir. 2003), *rehearing denied* (Apr. 25, 2003); *petition for cert. filed*, 72 U.S.L.W. 3106 (U.S. Jul. 24, 2003) (No. 03-124). *Moba* stressed again that "[t]he test for compliance with § 112 has always required sufficient information in the original disclosure to show that the inventor possessed the invention at the time of the original filing . . . '[t]he written description requirement does not require the applicant to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. . . .'" *Moba*, 352 F.3d at 1320-1321, 66 USPQ2d at 1439, quoting *Union Oil Co. of Cal. V. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000).

Applicants respectfully submit that all of the presently pending claims meet the written description requirement as elucidated by these Federal Circuit decisions as well as the USPTO's Written Description Guidelines. The Examiner's argument that the written description requirement is not met because "Applicants have claimed a genus of polypeptides that have no common function" is misplaced. Each of the claims specifies an IFN-β polypeptide variant exhibiting IFN-β activity. As discussed above, the specification clearly defines such activity and

describes methods for determining whether an IFN-β polypeptide variant exhibits IFN-β. Furthermore, the specification demonstrates that numerous specific variants comprising introduced N-glycosylation sites within the claimed genus exhibit IFN-β activity. For example, Example 5 demonstrates that an IFN-β polypeptide variant comprising the introduced N-glycosylation site F111N+R113T exhibits IFN-β activity as shown by the primary assay. Example 6 establishes that an IFN-β polypeptide variant comprising the introduced N-glycosylation site Q49N+Q51T exhibits IFN-β activity as shown by the primary assay. See also the additional examples provided in the specification at, *e.g.*, pages 83-120.

The Examiner's assertions that the specification fails to disclose if there are multiple glycosylation sites and fails to indicate how an amino acid substitution adjacent a glycosylation site will affect the glycosylation site also lack merit. The specification clearly explains that an N-glycosylation site has the sequence N-X'-S/T/C-X", wherein X' is any amino acid residue except proline, X" is any amino acid residue that may or may not be identical to X' and preferably is different from proline, N is asparagine and S/T/C means either serine, threonine, or cysteine, preferably serine or threonine, and most preferably threonine. *See, e.g.*, page 19, lines 7-9 and page 11, line 32 to page 12, line 6. The specification points out (*e.g.*, on page 19, lines 26-27) that wild-type human IFN-β contains naturally occurring N-glycosylation site defined by N80 and T82 (*i.e.*, N80-E81-T82) (here E81 is X'). Given the definition of an N-glycosylation site, one skilled in the art would readily recognize an N-glycosylation site in the sequence of wild-type human IFN-β (SEQ ID NO:2). The specification also plainly explains that glycosylation at a given N-glycosylation site of an IFN-β molecule may be increased by modifying an amino acid residue at a position -1 relative to the N-glycosylation site (*i.e.*, at the position -1 relative to asparagine (N)). See the specification, including at, but not limited to, *e.g.*, page 18, line 14 to page 28, line 10.

Furthermore, the Examiner's arguments that "[i]t is not clear what substitutions will retain commons functions" and "[i]t is also how [sic] and what functions will be affected by the glycosylation" are improper. Predictability is not the legal standard or test for such a rejection. The issue is not whether Applicants provided experimental functional data for each sequence that falls within the scope of a claim, but whether Applicants have presented sufficiently detailed and

relevant identifying characteristics, such as structure, function, chemical properties, *etc.*, or a combination thereof, such that one of skill would understand, based upon reading the specification, that Applicants were in possession of a claimed polypeptides or compositions thereof at the time of filing. Here, the written description requirement of amended claim 88 and claims dependent thereon, is plainly met. Amended claim 88, for example, more particularly specifies an IFN-β polypeptide variant exhibiting interferon β activity which comprises a sequence which differs from the wild-type human interferon β sequence SEQ ID NO:2 in no more than 15 amino acid residues and has at least one introduced N-glycosylation site comprising two amino acid substitutions relative to SEQ ID NO:2 selected from the group consisting of Q49N+Q51T/S and F111N+R113T/S and an amino acid substitution at position –1 relative to at least one of the introduced N-glycosylation site(s). Applicants' disclosure clearly provides sufficiently detailed and relevant identifying characteristics of the claimed genus. Applicants provide specific chemical structural features common to members of the genus that distinguish them from others, disclose that each such member has IFN-β activity, disclose a specific correlation between the claimed structures and the asserted function, and provide a specific description of the assays one can use to test whether a particular structural sequence has the asserted function. The disclosed function is sufficiently correlated to a particular structure, since the IFN-β activity of an IFN-β polypeptide variant comprising at least one of the introduced N-glycosylation sites defined by amended claim 88 can be readily determined, as shown in the methods set forth in the specification. Based on Applicants' detailed disclosure, one of skill in the art would certainly have recognized that Applicants were in possession of the claimed polypeptides and compositions thereof at the time of filing.

The Examiner's assertion that the written description requirement is not met because "the specification does not disclose all possible variants (with up to 15 amino acid residue changes) of interferon-β" is also improper. The law is clear that all possible variants of a claimed genus need not be described to satisfy the written description requirement. Rather, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by

functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. Here, Applicants' disclosure explicitly describes a sufficient number of representative species of the genus defined by claim 88. A number of representative species of the claimed genus have been reduced to practice as shown in the specification, including at, but not limited to, *e.g.*, Examples 5-9 and 13-23. For instance, Example 5 demonstrates that an IFN-β polypeptide variant comprising the introduced N-glycosylation site F111N+R113T exhibits IFN-β activity as evidenced by the primary assay. Example 6 shows that an IFN-β polypeptide variant comprising the introduced N-glycosylation site Q49N+Q51T exhibits IFN-β activity as established by the primary assay. Example 7 demonstrates that an IFN-β polypeptide variant comprising the two introduced N-glycosylation sites Q49N+Q51T and F111N+R113T exhibits IFN-β activity as shown by the primary assay. Example 17 demonstrates that the IFN-β polypeptide variant comprising the introduced N-glycosylation site Q49N+Q51T and an amino acid substitution at position Q48 relative to SEQ ID NO:2 exhibit IFN-β activity and an increased amount of glycosylation at this N-glycosylation site. See also Examples 8-9, 13-16, and 18-23.

Moreover, Applicants' specification discloses additional specific IFN-β polypeptide variants of the claimed genus which possess the defined common structural features and correlated functional activity (*i.e.*, variants exhibiting IFN-β activity that differ from SEQ ID NO:2 in no more than 15 amino acid residues and which comprise at least one introduced N-glycosylation site comprising two specific amino acid substitutions relative to SEQ ID NO:2 and a substitution at position -1 relative to at least one such N-glycosylation site). The specification provides detailed guidance and examples as to how to make polypeptide variants possessing the necessary common structural features and screen such polypeptide variants for the asserted IFN-β activity. See the specification, including at, but not limited to, *e.g.*, page 5, line 2 to page 10, line 4; page 16, line 20 to page 17, line 8; page 20, line 14 to page 26, line 32; page 28, line 13 to page 29, line 4; page 43, lines 30-32; page 46, line 15 to page 48, line 31; and the Examples section (pages 83-120).

In summary, Applicants' teachings of the common structural features possessed by the claimed polypeptides and methods for making them, details of the functional characteristics of such polypeptides, and disclosed correlation between such structures and the asserted function, coupled with the detailed methods describing how to test for functional polypeptides using the assays provided in the specification, support the conclusion that Applicants sufficiently described and were in possession of the invention as claimed at the time of filing. Based on these teachings, one skilled in the art would undoubtedly have understood that Applicants were in possession of the claimed polypeptides and compositions thereof at the time of filing the application.

For at least these reasons, Applicants submit that the rejection of claim 88 and claims dependent thereon is improper and nevertheless overcome by the amendments to claim 88 and respectfully request that it be withdrawn.

B. The Claims Are Sufficiently Enabled

Claims 88-99 were rejected under 35 USC § 112, first paragraph, because the specification, while being enabling for an interferon-β variant with substitutions at K19R+K45R+K123R of the wild type protein which has antiviral activity, allegedly does not reasonably provide enablement for all variants contemplated. Office Action, pages 6-7. The Examiner takes the position that "it is also unclear what activity if any will be associated with the specific interferon-β variants" and "[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." *Id.* at page 7.

The Examiner finds that "the specification fails to provide any guidance regarding the changes/modifications contemplated and yet retain the functions(s) of the interferon-β variants claimed" and "detailed information regarding the structural and functional requirements of the disclosed variant protein is lacking." *Id.* The Examiner also contends that "Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (*e.g.*, such as by amino acid substitutions or deletions) and the

nature and extent of changes that can be made in these positions" and the specification "is merely an invitation to the artisan to use the current invention as a starting point for experimentation." *Id.* The Examiner concedes that "the specification outlines art-recognized procedures for producing and screening for active variants," but asserts that there is "not adequate guidance as to the nature of active derivatives that may be constructed." *Id.*

The Examiner further finds that the "instant disclosure fails to disclose which if any functions of the interferon-β activities will remain or required [sic] after the mutation of the polypeptide" and "[i]t is also unclear what are functions that will be enhanced following the glycosylation of interferon-β." *Id.* at page 8. Based on these findings, the Examiner asserts that "predicting which variants would retain the functions of the protein is well outside the realm of routine experimentation" and "[t]hus, undue amount of experimentation would be required to generate changes/modifications contemplated and yet retain the function of the proteins claimed." *Id.*

The Examiner is of the view that "the specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences" and that "the amount of experimentation required to make and/or use the full scope of the claimed sequence would require trial and error experimentation to determine the functional sequences." *Id.* The Examiner finally asserts that "[g]iven the breadth of claims 88-99 in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior art of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention." *Id.* The rejection of claims 90-91 and 93 has been mooted by cancellation of those claims without prejudice. The rejection of claims 89, 92, and 94-99 is respectfully traversed in part and overcome in part as follows.

Courts have outlined several factors that may be considered in determining whether a specification does not satisfy the enablement requirement. These include: (1) the breath of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation

needed to make or use the invention based on the content of the disclosure. *See, e.g., In re Wands*, 858 F.2d 731, 737; 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

A review of these factors as applied to amended claim 88, and claims dependent thereon, confirms that these claims are fully enabled. As amended, claim 88 specifies an IFN-β polypeptide variant exhibiting IFN-β activity which comprises a variant sequence which differs from the wild-type human IFN-β sequence SEQ ID NO:2 in no more than 15 amino acid residues. The variant sequence comprises at least one introduced N-glycosylation site comprising two amino acid substitutions relative to SEQ ID NO:2 selected from the group consisting of Q49N+Q51T/S and F111N+R113T/S, and an amino acid substitution at position –1 relative to at least one of the introduced N-glycosylation site(s). Contrary to the Examiner's assertions, the specification provides detailed guidance regarding the structural and functional requirements of the claimed IFN-β polypeptide variants. As clearly set forth in the specification, the claimed IFN-β polypeptide variant differs from SEQ ID NO:2 by no more than 15 amino acid residues and comprise at least one introduced N-glycosylation site comprising two particular amino acid substitutions relative to SEQ ID NO:2 selected from Q49N+Q51T/S and F111N+R113T/S. In addition, each IFN-β polypeptide variant must have an amino acid substitution at position –1 relative to at least one of the introduced N-glycosylation site(s). Furthermore, each IFN-β variant must exhibit IFN-β activity and methods for determining whether a variant has such activity are expressly disclosed in the specification (*see, e.g.*, pages 83-88). Applicants provide explicit descriptions of specific active IFN-β variants possessing the recited substitutions and also provide detailed guidance as to amino acid modifications of human IFN-β (SEQ ID NO:2) than can be made while retaining IFN-β activity. See the specification, including at, but not limited to, *e.g.*, page 5, line 2 to page 10, line 4; page 16, line 20 to page 17, line 8; page 20, line 14 to page 26, line 32; page 28, line 13 to page 29, line 4; page 43, lines 28-32; page 46, line 15 to page 48, line 31; and the Examples section (pages 83-120).

Contrary to the Examiner's contention that the specification lacks working examples, numerous working examples are provided. Many of the twenty-three Examples presented in the specification (see pages 83-120) plainly demonstrate active variants of the invention possessing

the particular structural characteristics, amino acid substitutions and IFN-β activity specifically defined by amended claim 88.

Additionally, the level of one of ordinary skill in the art was high in the art at the time the application was filed. Given the nature of the invention and the state of the prior art in the field at the time of filing, and the considerable direction and guidance in the specification as outlined above, one of ordinary skill in the art would certainly have been readily able to make and use the IFN-β polypeptide variants defined by claim 88 and the claims dependent thereon.

Moreover, even if some experimentation would have been necessary to make and use the claimed polypeptide variants, such experimentation would clearly not support an enablement rejection of claims 88 or any claim dependent thereon. *Wands*, 858 F.2d at 737; *Atlas Powder Co. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569 (Fed. Cir, 1984). It has long been established that enablement is not precluded even if some experimentation is required, provided that the amount of experimentation is not "unduly extensive." *Atlas Powder*, 750 F.2d at 1576. The correct test for enablement is not whether some "trial and error experimentation to determine the functional sequences" is required (as the Examiner alleges), but whether, if experimentation is necessary, it is undue. *Wands*, 858 F.2d at 737; 8 USPQ2d at 1404. Moreover, the fact that experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation. *Id.*

In this instance, based upon the detailed teachings of the specification (including the abundant guidance provided in the specification regarding specific IFN-β polypeptide variants possessing the asserted activity and methods for making IFN-β polypeptide variants which have the recited substitutions and IFN-β activity), the particularly defined nature of the invention, the numerous working examples, the state of the art, and the high level of skill in the art at the time the application was filed, one of ordinary skill in the art would have been reasonably able to make and use the polypeptides set forth in amended claim 88, and the claims dependent thereon, without unduly extensive experimentation.

For at least these reasons, Applicants submit the rejection is improper and nevertheless overcome by the amendment to the claims. Withdrawal of the rejection is respectfully requested.

V. NO ADDITIONAL CLAIMS FEES DUE

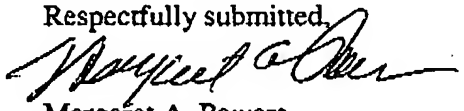
Applicants believe no additional fees are required for the new dependent claims 109-117, since 87 claims were originally filed in the application, and owing to the presence of multiple dependent claims (for which the surcharge was paid), for fee calculation purposes, these amounted to a total of 199 claims (11 independent). With the present Amendment, a total of 18 claims are pending, of which one claim is independent.

Therefore, it is believed that no additional claim fees are due with this Amendment. A fee pursuant to Applicants' request for extension of time is due and the Commissioner is authorized to deduct such fee and any additional fees required for entry of this Amendment from the undersigned's Deposit Account No. 50-0990. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

CONCLUSION

In view of the foregoing, Applicants believe that all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 298-5809.

Respectfully submitted,



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